

CLAIMS:

1. Isolated RP-factor.
- 5 2. The factor of claim 1 which is a secreted RP-factor.
3. The factor of claim 1 which is a non-secreted RP-factor (e.g. a cell-associated or cytosolic factor).
- 10 4. The factor of any one of the preceding claims which is derived from a bacterium (e.g. a pathogenic bacterium).
5. The factor of claim 4 which is derived from:
  - (i) a high G+C Gram-positive bacterium; or
  - 15 (ii) a low G+C Gram-positive bacterium (for example *Streptococcus* spp., *Staphylococcus* spp., *Listeria* spp., *Bacillus* spp., *Clostridium* spp. and *Lactobacillus* spp.).
6. The factor of claim 5(i) which is derived from:
  - 20 (a) *Micrococcus* spp. (e.g. *M. luteus*); or
  - (b) *Mycobacterium* spp. (for example a fast- or slow-growing mycobacterium, e.g. *M. tuberculosis*, *M. leprae*, *M. smegmatis* or *M. bovis*); or
  - (c) *Streptomyces* spp. (e.g. *S. rimosus* and *S. coelicolor*); or
  - (d) *Corynebacterium* spp. (e.g. *C. glutamicum*).
- 25 7. A homologue, derivative, allelic form, species variant, mutein or equivalent of the factor of any one of the preceding claims.
8. A factor of any one of the preceding claims which comprises (or consists of) the  
30 RP-factor signalling domain.

9. A factor of any one of the preceding claims which comprises (or consists of) the RP-factor specificity-determining domain.
10. Recombinant RP-factor, wherein the RP-factor is for example as defined in any one of the preceding claims.
11. A pharmaceutical composition (e.g. a vaccine) comprising an RP-factor as an active ingredient (for example the factor (or homologue, derivative, allelic form, species variant, mutein or equivalent) as defined in any one of the preceding claims), the RP-factor for example being present at a concentration sufficient to confer biological activity on the pharmaceutical composition.
12. An RP-factor (for example the factor (or homologue, derivative, allelic form, species variant, mutein or equivalent) or pharmaceutical composition as defined in any one of the preceding claims) which is:
- (a) for use in therapy (e.g. immunotherapy), diagnosis or prophylaxis; and/or
- (b) in a pharmaceutical excipient, a unit dosage form or in a form suitable for local or systemic administration.
13. An antibody (or antibody derivative) specific for the factor (or homologue, derivative, allelic form, species variant, mutein or equivalent) as defined in any one of the preceding claims.
14. The antibody of claim 13 which is:
- (a) for use in therapy (e.g. immunotherapy), diagnosis or prophylaxis; and/or
- (b) in a pharmaceutical excipient, a unit dosage form or in a form suitable for local or systemic administration.
15. Isolated RP-factor receptor or convertase.
16. The receptor/convertase of claim 15 which is derived from a source as defined

in any one of claims 4-6.

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17. A homologue, derivative, allelic form, species variant, mutein or equivalent of the receptor/convertase of claim 15 or 16.
18. Recombinant RP-factor receptor/convertase, wherein the receptor/convertase is for example as defined in any one of claims 15-17.
- 10 19. A pharmaceutical composition (e.g. a vaccine) comprising the receptor/convertase (or homologue, derivative, allelic form, species variant, mutein or equivalent) as defined in any one of claims 15-18.
- 15 20. The receptor/convertase (or homologue, derivative, allelic form, species variant, mutein or equivalent) or pharmaceutical composition as defined in any one of claims 15-19 which is:
- (a) for use in therapy (e.g. immunotherapy), diagnosis or prophylaxis; and/or
- (b) in a pharmaceutical excipient, a unit dosage form or in a form suitable for local or systemic administration.
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21. An antibody (or antibody derivative) specific for the receptor (or homologue, derivative, allelic form, species variant, mutein or equivalent) as defined in any one of claims 15-20.
- 25 22. The antibody of claim 21 which is:
- (a) for use in therapy (e.g. immunotherapy), diagnosis or prophylaxis; and/or
- (b) in a pharmaceutical excipient, a unit dosage form or in a form suitable for local or systemic administration.
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23. An RP-factor antagonist or inhibitor.

24. The antagonist or inhibitor of claim 23 which comprises:
- (a) the antibody of claim 13, 14, 21 or 22; and/or
  - (b) the receptor of claims 15-20; and/or
  - (c) an RP-factor mutein which comprises an altered RP-factor specificity-determining domain or which lacks a functional signalling domain.
25. The antagonist or inhibitor of claim 23 or 24 which is:
- (a) for use in therapy (e.g. immunotherapy), diagnosis or prophylaxis; and/or
  - (b) in a pharmaceutical excipient, a unit dosage form or in a form suitable for local or systemic administration.
26. An RP-factor agonist, activator or mimetic.
27. The agonist, activator or mimetic of claim 26 which comprises:
- (a) the antibody of claim 21 or 22; and/or
  - (b) an RP-factor mutein comprising (or consisting of) an RP-factor specificity-determining domain; and/or
  - (c) an RP-factor mutein comprising (or consisting of) an RP-factor signalling domain; and/or
  - (d) an RP-factor convertase; and/or
  - (e) operably coupled combinations of any of (a)-(d).
28. The agonist, activator or mimetic of claim 27 which is:
- (a) for use in therapy (e.g. immunotherapy), diagnosis or prophylaxis; and/or
  - (b) in a pharmaceutical excipient, a unit dosage form, in a form suitable for local or systemic administration or in admixture with an antibiotic.
29. The agonist, activator or mimetic of claim 28 which is for use in adjunctive

therapy (for example in combination with an antibiotic).

- 5 30. Isolated nucleic acid encoding the RP-factor (or homologue, derivative, allelic form, species variant, mutein or equivalent thereof) or RP-factor receptor as defined in the preceding claims.
31. A vector (e.g. an expression vector) comprising the nucleic acid of claim 30.
- 10 32. A host cell comprising the vector of claim 31.
33. A culture or transport medium comprising an RP-factor (e.g. the factor (or homologue, derivative, allelic form, species variant, mutein or equivalent) as defined in the preceding claims), for example comprising a culture supernatant containing an RP-factor.
- 15 34. A nucleic acid probe comprising nucleic acid complementary to the nucleic acid of claim 30.
- 20 35. A diagnostic kit comprising an RP-factor (or homologue, derivative, allelic form, species variant, mutein or equivalent), receptor, antibody, probe, culture supernatant or culture medium as defined in any one of the preceding claims.
36. Antisense DNA corresponding to the nucleic acid of claim 30.
- 25 37. A process for producing an antimicrobial drug comprising the steps of:
- (a) providing an RP-factor receptor;
  - (b) providing candidate drugs;
  - (c) screening the candidate drugs by contacting the RP-factor receptor with one of the candidate drugs and determining the affinity of the candidate
- 30 drug for the RP-factor receptor, wherein the affinity is an index of antimicrobial activity, and optionally

(d) synthesising or purifying a drug having antimicrobial activity on the basis of the identity of the candidate drug screened in step (c).

38. A process for producing an antimicrobial drug comprising the steps of:
- 5 (a) providing an RP-factor receptor;  
(b) providing a candidate drug;  
(c) providing an RP-factor;  
(d) screening the candidate drugs by contacting the RP-factor receptor with one of the candidate drugs in the presence of the RP-factor, and then  
10 determining the ability of the candidate drug to compete non-productively with the RP-factor for binding to the RP-factor receptor, wherein the competitive binding ability is an index of antimicrobial activity, and optionally  
(e) synthesising or purifying a drug having antimicrobial activity on the basis of the identity of the candidate drug screened in step (d).
- 15 39. An antimicrobial drug produced by (or obtainable by) the process of claim 37 or 38, or a derivative thereof.
40. A method for determining the microbiological quality of a product (e.g. a  
20 foodstuff, pharmaceutical preparation or medical product) comprising the step of contacting a sample of the product with an RP-factor (for example, an RP-factor as defined in the preceding claims).
41. A method of culturing bacterial (e.g. mycobacterial) cells, comprising the step  
25 of incubating the cells in a culture medium comprising an RP-factor (for example, an RP-factor as defined in the preceding claims).
42. An *ex vivo* method of diagnosis, comprising the step of contacting a biological  
30 sample with an RP-factor (for example, an RP-factor as defined in the preceding claims).

43. The method of claim 42 wherein the biological sample is incubated with a culture or transport medium as defined in claim 33.
44. A method of:
- 5 (a) stimulating the growth of a microorganism; and/or  
(b) resuscitating a dormant, moribund or latent microorganism;  
comprising the step of contacting the microorganism with an RP-factor (for example, an RP-factor as defined in the preceding claims).
- 10 45. A process for producing the RP-factor or RP-factor receptor of the invention comprising the steps of:
- (a) culturing the host cell of claim 32, and  
(b) purifying the factor or receptor from the cultured host cells (e.g. from a culture supernatant or cell fraction).
- 15 46. A process for producing the RP-factor or receptor of the invention comprising the steps of:
- (a) probing a gene library with a nucleic acid probe which is selectively hybridizable with the nucleic acid of claim 30 to produce a signal which  
20 identifies a gene that selectively hybridises to the probe;  
(b) expressing the gene identified in step (a) (for example by cloning into a host cell, e.g. according to a process as defined in claim 45) to produce the factor or receptor.
- 25 47. An RP-factor or receptor obtainable by the process of claim 45 or 46.

48. A process for producing a library of biomolecules comprising the steps of:
- (a) providing a sample (e.g. a soil, marine, food, freshwater, tissue or organism-derived);
  - (b) incubating the sample in a culture medium comprising an RP-factor  
5 (for example, an RP-factor as defined in the preceding claims or a culture supernatant comprising an RP-factor) to produce a microbial culture;
  - (c) isolating microorganisms from the culture of step (b).
49. The process of claim 48 further comprising the step of screening the isolated  
10 microorganisms for those which elaborate one or more biomolecules of interest (for example a metabolite, enzyme, antibiotic (e.g. antiviral, antibacterial or antifungal agent) or toxin).
50. A biomolecule produced by (or obtainable by) the process of claim 48 or 49, or  
15 a derivative thereof.
51. A process for producing a library of microorganisms (e.g. bacteria) comprising the steps of:
- (a) providing a sample (e.g. a soil, marine, food, freshwater, tissue or  
20 organism-derived sample);
  - (b) incubating the sample in a culture medium comprising an RP-factor (for example, an RP-factor as defined in the preceding claims or a culture supernatant comprising an RP-factor) to produce a microbial culture;
  - (c) isolating microorganisms from the culture of step (b); and optionally  
25 (d) culturing and/or mutagenising the microorganism.
52. A microorganism produced by (or obtainable by) the process of claim 51, or a derivative (e.g. mutant) thereof.



53. Use of a culture supernatant (or fraction or extract thereof) containing an RP-factor for:
- (a) diagnosis, prophylaxis or therapy; or
  - (b) producing a library of microorganisms (e.g. according to the method of claim 51); or
  - (c) producing a library of biomolecules (e.g. according to the method of claim 48); and/or
  - (d) resuscitating a dormant, moribund or latent pathogen (e.g. according to the method of claim 44(b)).
54. A culture supernatant (or fraction or extract thereof) containing an RP-factor for use in therapy, prophylaxis or diagnosis.
55. An *ex vivo* method of diagnosis comprising the step of incubating a sample with a culture supernatant (or fraction or extract thereof) containing an RP-factor (or an RP-factor as defined in any one of the preceding claims) at a concentration sufficient to promote the recovery of microorganisms from the sample by culture.
56. The method of claim 55 wherein the sample:
- (i) is from an accessible body site, for example a mucous membrane of the vagina, anus, nose, urethra, cervix, skin, conjunctiva, mouth or throat; and/or
  - (ii) comprises a fluid or semi-solid (for example a bodily fluid or semi-solid, e.g. discharge, vomit, secretion, excreta, sputum or blood); and/or
  - (iii) comprises a solid (e.g. stool, tissue, food or biopsy sample); and/or
  - (iv) comprises a culture (e.g. a microbiological culture).
57. A live vaccine comprising an attenuated microbe, which microbe bears a mutation in a gene encoding (or regulating the expression or activity of) one or more RP-factors.

58. The vaccine of claim 57 wherein the microbe selected from any of: an actinomycete, mycobacterium (for example *M. tuberculosis*, *M. leprae*, *M. bovis* (e.g. *M. bovis* BCG) and *M. avium*), *Corynebacterium* spp. (e.g. *Corynebacterium diphtheriae*), *Tropheryma whippelii*, *Nocardia* spp. (e.g. *Nocardia asteroides* and *Nocardia brasiliensis*), *Streptomyces* spp. (e.g. *Streptomyces griseus*, *Streptomyces paraguayensis* and *Streptomyces somaliensis*), *Actinomadura* spp., *Nocardiopsis* spp., *Rhodococcus* spp., *Gordona* spp., *Tsukamurella* spp. and *Oerskovia* spp., a pathogenic high G+C Gram-positive bacterium and a pathogenic low G+C Gram-positive bacterium (for example *Streptococcus* spp., *Staphylococcus* spp., *Listeria* spp., *Bacillus* spp., *Clostridium* spp. and *Lactobacillus* spp.).
59. The vaccine of claim 57 or claim 58 wherein the mutation is selected from any of: frameshift, deletion, insertion and/or substitution mutations.
60. The vaccine of any one of claims 57-59 wherein the mutation:
- (a) comprises a null mutation (e.g. a non-reverting null mutation); and/or
  - (b) prevents growth of the microbe; and/or
  - (c) results in the expression of a mutant RP-factor having altered specificity (e.g. in which the specificity-determining domain has been mutated or modified) and/or which lacks a functional signalling domain.